REVIEW ARTICLE

TUMORS OF THE HAIR FOLLICLE

Tumors of the Hair Follicle

A Review

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THE BIOLOGY OF HAIR GROWTH is so remarkably complex that it is truly extraordinary so little goes wrong with the hair follicle. Numerically, the opportunity for disorder is immense, for on the scalp alone there are 100,000 to 150,000 individual follicles, while over the remainder of the body there may be several times that number. In humans each follicle undergoes an asynchronous and variable growth cycle which is genetically programmed to grow scalp hair to about 1 meter, while keeping facial, body, axillary, and pubic hair appropriately stylized and at a conveniently manageable length. Similar to the epithelium of the small intestine and the myeloproliferative cells of the bone marrow, growing (anagen) hair matrix is one of the most rapidly proliferating tissues in the body. The single pool of stem cells which forms the matrix of the hair bulb, in prodigy of controlled differentiation, produces an elaborately structured and orderly concentric array of six morphologically different cell layers: the medulla, cortex, and cuticle of the hair as well as the three layers of the inner sheath. Moreover, in pigmented hairs, the bulbar melanocytes are integrated with only two of the six proliferating cell lines—supplying pigment to the cells of the cortex and medulla but not to the cells of the hair cuticle or the inner sheath.[1] As the follicle cycles into a resting phase (telogen), these melanocytes reduce their dendritic processes and apparently remain in a dormant state until called upon to once again become functional, with the onset of new growth.[2] In the upper part of the follicle the external root sheath is continuous with the epidermal component of the follicle, the infundibulum, which extends from the level of the epidermis to the opening of the sebaceous duct. Within this area the epithelial cell of the hair sheath is indistinguishable from the epidermal keratinocyte. It is this infundibular zone which is subject to many of the same environmental influences as is the epidermis and which presumably gives rise to some of the basal cell carcinomas, keratoacanthomas, and infundibular (epidermoid) cysts, which will not be considered here.

Each renewal or cycle of hair growth requires the inductive effect of a dermal papilla. At the onset of each new cycle there is a recondensation of

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papillary mesenchyme before growth and differentiation of telogen germinal epithelium begins. This mesenchymal element is the determining factor in differentiation, for the epithelium itself is indifferent. The hair follicle is, therefore, a highly integrated system of epithelial and mesenchymal interaction which has no counterpart elsewhere in adult human tissue.

The biologic sensitivity of the proliferating hair bulb is well known. There is a long list of hormonal, nutritional, metabolic, and toxic events which can cause one or another alterations of normal hair growth: reduced growth rate, altered hair structure, partial cyclic synchrony, or hair loss (defluvium). From the viewpoint of the oncologist, however, perhaps the most interesting observation to be made of the proliferative compartment of the hair and of its inductive mesenchyme is that there are very few primary neoplasms attributable to it. Where are the carcinomas of hair matrix, the melanomas of the hair bulb, and the mesenchymal tumors of the dermal papilla? Among the millions of human beings under some degree of medical scrutiny, none of these neoplasms have apparently been described with certainty, or if so, only one or two exist as curiosities. It is also a matter of record that relatively few benign tumors of the nonepidermal follicle have been recognized, described, and variously classified. In contrast to the gut and the bone marrow, the pilary system has apparently evolved a striking resistance to oncogenic stimuli, either because of a relatively protected anatomic location or unknown biologic factors or possibly due to both of these. It has only been in the last decade or so that primary neoplasms of the hair follicle, other than those common to the epidermis, have been given recognition as a group,[3,4] and it is only after this period of study and description that a comprehensive review can be undertaken and a reasonable nosology suggested.

A first consideration in the histogenesis of tumors of the hair follicle is the possible origin of adult or of stem cells within the epithelial integument which may be targets for neoplastic transformation. Theoretically, there are at least three forms of hair germ or trichoblastic epithelium. Primary hair germ, the epithelial anlage of the normal pilosebaceous unit, appears about the ninth week of embryonic life. Under the inductive influence of somatic mesenchyme, growth and differentiation of the pilosebaceous complex continues until the first generation of hairs broaches the epidermal surface between the thirteenth and fifteenth weeks. During the earliest embryonic phase of pilar histogenesis, a dense ball of epithelial cells buds downward from the primitive periderm. In sagittal section, these buds display a distinct and orderly palisade of tightly packed basal cells. This most primitive morphologic marker of the first generation hair

follicle is recapitulated in several neoplasms of hair germ. (See trichoblastic fibroma).

The participation of primary epithelial germ in the histogenesis of hamartomas and primary neoplasms of hair follicles is probably limited to a few rare localized or generalized hamartomatous conditions clinically manifest at birth or shortly thereafter.

A second form of hair germ is telogen or secondary germ. At the conclusion of the regressive or catagen phase of the normal hair cycle, a small cord or mass of undifferentiated epithelial cells extends from the remnants of the outer sheath to the presumptive dermal papilla. There is little growth or differentiation of these cells as the follicle rests during telogen. However, with the onset of anagen there is new growth and differentiation. Activation and proliferation of telogen germ are followed by specialization of hair matrix cells which form hair shaft, the cuticular layer, and the layers of the inner sheath. Primary hair germ and telogen germ are probably separate only in time, as telogen germ is presumably the linear descendent of primary germ.

The histogenesis of hair follicle neoplasms is not specifically associated with telogen germ, but there are a number of candidates for such origin including trichomatricoma and trichoblastoma.

A third form of hair germ, however, is required to fully explain the morphogenesis of certain other pilar neoplasms. Epigenic germ, a theoretical consideration derived from classic embryology, indicates that any cell in the proliferative compartment of the epithelial integument of either epidermal or adnexal origin can, under appropriate stromal induction, undergo some degree of follicular differentiation.

Epigenic hair germ has been experimentally established as a biologic system. Kollar [5,6] has induced hair follicles in glabrous foot pad and tooth epithelium of mice by appropriate transplantation of inductive mesodermal tissues from hair-bearing areas. This work established that stromal elements are the obligatory determinants and that the nature of the inductive response is a specific function of the mesodermal component. New follicles derived from outer sheath epithelium, as found in trichofolliculoma, may be an example of induction of epigenic germ.

Matrix cells have long been recognized as capable of disorganized growth. In addition, reserve cells of the outer sheath and possibly the basal cells of the epidermis can proliferate and specialize to form distinctive keratinous epithelial tumors without obvious stromal induction. This pattern of keratinization (tricholemmal keratinization) replicates that of the outer sheath in several histologically different tumors. Stromal elements of the follicle are also to be considered as targets for neoplastic

change, however, with the exception of tumors of the dermal papilla and the hair disc, description of stromal tumors (fibromas, leiomyomas) has evolved along more or less conventional lines (Table 1).

Hamartomas of Hair Germ

Becker's nevus (pigmented hairy nevus) occurs as a localized patch of coarse terminal body hair on the upper back or shoulders in adult males. Associated epidermal pigmentation is variable in intensity. The slight histologic changes in this lesion are primarily epidermal, usually with

Table 1—A Histogenetic Classification of Tumors and Cysts of the Hair Follicle

Hamartomas of hair germ
Localized with limited morphodifferentiation
Trichoepithelioma
Hamartomas of the nevus sebaceous complex
Localized with advanced morphodifferentiation
Trichofolliculoma
Basal cell hamartoma
Congenital vellus hamartoma
Generalized, without morphodifferentiation
Generalized, with morphodifferentiation
Tumors of hair germ
Epithelial trichogenic tumors without induction
Trichoblastoma
Epithelial trichogenic tumors with induction
Trichoblastic fibroma
Trichogenic trichoblastoma
Mesenchymal trichogenic tumors
Trichogenic myxoma
Tumors of hair matrix
Trichomatricoma (pilomatricoma)
Carcinoma of hair matrix (matrical carcinoma)
Tumors of external hair sheath (tricholemma)
Tricholemmal cyst (pilar cyst)
Proliferating tricholemmal tumor
Tricholemmal keratosis
Tricholemmoma
Tricholemmal carcinoma
Tumors of perifollicular mesenchyme
Trichodiscoma
Perifollicular fibroma
Pilar leiomyoma (trichomyoma)
Tumors of the intraepidermal follicle and infundibulum
Inverted follicular keratosis (acrotrichoma)
Tumor of follicular infundibulum
Dilated pore
Tumors of miscellaneous type
Trichoadenoma
Trichoma

some degree of acanthosis.[7] True nevus cells are not found. It has not been determined if this lesion is due to a quantitative increase in number of terminal hair follicles per unit area or is an ectopic area of usually marked vellus to terminal hair transformation. Becker's nevus almost certainly is not a hamartoma of the hair follicle in the usual nosologic sense.

Occasionally, small congenital nodules are found on the head and neck which are composed of numerous tightly packed but well-formed vellus follicles (Figures 1 and 2).[8,9] These are best termed *congenital vellus hamartomas* and are probably the result of an excessive localized proliferation of primary hair germ at a very early stage of development which is then followed by normal histodifferentiation.

Localized hamartomas of hair germ with very limited follicular morphodifferentiation are represented by the trichoepithelioma either solitary or multiple. Other examples are occasionally encountered as a component of nevus sebaceous (Figures 3 and 4).

Localized hamartomas with advanced follicular differentiation are of two types: a) trichofolliculoma and b) superficial basal cell hamartoma. The latter is characterized clinically by symmetrical periorbital papules, and histologically by a plate-like proliferation of basal cells with varying degrees of follicular differentiation.[10]

Generalized hamartomas of hair germ resembling trichoepitheliomas without morphodifferentiation are described in a unique case with aminoaciduria and progressive alopecia.[11]

Trichoepithelioma

Trichoepitheliomas are benign cutaneous epithelial-mesenchymal tumors best classified as poorly differentiated hamartomas of hair germ (trichogenic hamartomas).[12] They are characteristically either multiple (epithelioma adenoides cysticum) or solitary. If multiple, trichoepithelioma may be familial, with transmission as an autosomal dominant trait.[13] One-half to two-thirds of patients with multiple lesions will have a positive family history. Onset may be during childhood or during adult life. A conspicuous increase in the number of lesions can occur during puberty.

Multiple trichoepitheliomas appear as small, discrete, often grouped, skin-colored nodules and papules with a tendency to appear on the upper lips and nasolabial folds. They may also be distributed on the scalp, upper extremities, and trunk. Individual lesions on the face and neck rarely exceed 0.5 cm but may be larger elsewhere. Growth is limited, and a stationary size is generally reached after a few years. Malignant transformation, if it occurs, is extraordinarily rare although coexisting basal carcinoma has been reported.[14]

Solitary lesions present as nondescript asymptomatic nodules or papules with a similar predilection for the face and neck. They will commonly simulate basal cell carcinoma, a nevocellular nevus, or other benign lesion.

Genetic studies have suggested that the coexistence of dermal eccrine cylindromas and trichoepitheliomas in the same patient is due to a single autosomal dominant gene capable of phenotypic dimorphism and variable penetrance.[15] In such patients, although cylindromas are limited largely to the scalp and trichoepitheliomas are predominantly centrofacial, some microscopic fields may show adjacent cylindromas and trichoepitheliomas. Unlike the nevoid basal cell carcinoma syndrome, there has been no reported association with lesions in the other organ systems.

The detailed histologic features of trichoepithelioma are highly variable. Relatively constant and diagnostic findings include a) A well-circumscribed ovoid or spherical intradermal nodule composed of budding epithelial islands of poorly specialized basophilic keratinocytes which are encompassed and separated by a well-developed collagenous stroma; epithelium is arrayed in interconnecting strands and cellular islands are marginated by a peripheral nuclear palisade. b) Focal continuity with the epidermis. c) Formation of small keratinous cysts lined by flattened squamous cells containing keratohyaline granules and showing an abrupt zone of keratinization (Figures 5 and 6). On occasion, keratotic debris will undergo dystrophic calcification. Intracellular melanin may be present, and tonofibrils within epithelium can be demonstrated with polarized light and by electron microscopy.

Histologic variants include tumors composed exclusively of small nonkeratinizing basophilic cells, tumors composed predominantly of cystic spherical nodules composed of well-differentiated keratinocytes, trichoadenoma (Figures 7, 8),[16] rare tumors showing advanced stromal induction of hair follicles,[12] and rare tumors containing well-differentiated sebaceous [17] and apocrine epithelium.[18]

A syringoid variant,[12,19] found almost exclusively as a small solitary morpheaform plaque on the face of a child or young adult and is microscopically composed of long delicate epithelial strands and small calcified keratinous microcysts, may deserve a separate designation.

Paraffin section histochemistry has shown no differences between multiple and solitary tumors. Preparations for sulfhydryl groups were slightly positive in cyst keratin in some areas.[12] Frozen-section enzyme histochemistry has demonstrated similarities between the perifollicular stroma and dermal papilla of the normal follicle and the inductive stroma of trichoepithelioma,[20] thus substantiating a degree of stromal cytochemi-

cal specialization concordant with limited pilar induction. These findings, however, relate to histodifferentiation but not to histogenesis. The strong stromal reactions for alkaline phosphatase in both anagen follicles and trichoepithelioma can also be interpreted to differentiate trichoepithelioma from keratotic basal cell carcinoma but would be of practical value only if one were doing routine frozen-section enzyme histochemistry on suspected basal cell carcinomas.

Differentiation of the purely epithelial nonkeratinizing variants of trichoepithelioma from indolent basal cell carcinoma can be troublesome in routine preparations. In general, trichoepithelioma is surrounded by densely collagenized rather than myxoid stroma, nontraumatic surface erosion rarely occurs, division figures are uncommon, individual tumor cell necrosis is usually absent, and inflammation is inconsequential (Figures 9 and 10).

The histologic features of the nevoid basal cell carcinoma syndrome are essentially identical to those of the spectrum of basal cell carcinoma, with histochemical findings characteristic for basal cell neoplasms.

The histogenesis of trichoepithelioma, single or multiple, is uncertain. Serial sections often demonstrate multiple points of epithelial continuity with both the epidermis and the outer sheath. Using glucose-6-phosphate dehydrogenase (G-6-PD) mosaicism as a tracer in the study of multiple hereditary trichoepitheliomas, Gartler and others [21] determined that trichoepitheliomas from a G-6-PD heterozygote were composed of both normal and enzyme-deficient cells. Presumably, in hereditary trichoepithelioma, all the cells in the proliferative pool of adnexal and epidermal keratinocytes are sensitive to tumor induction, and therefore the inducing agent may affect a large target cell population having potentially different clonal characteristics. This would correlate quite well with the common morphologic observation of multiple points of continuity between tumor and normal epithelium.

Trichofolliculoma

Trichofolliculoma is a benign highly structured hamartoma of the pilosebaceous unit characterized by one or more large cystic follicles with smaller radiating follicular structures.[22,23] The investing stroma is considered inductive when hairs are formed. Synonyms include folliculoma and hair follicle nevus.

The clinical presentation in about half of the cases is a small elevated plaque or flattened nodule with a pore or depression. Occasionally, a comedone or a sebum-like exudate has been described. A tuft of vellous

hairs, white or pigmented, or a wool-like wisp of trichoidal keratin may protrude from the lesion and serves as a reliable sign for clinical recognition. In cases reported thus far, trichofolliculoma has been confined to the head and neck, most commonly on the skin of the face. All examples have been solitary. Although data for age and sex distribution are probably biased by the large series from the Armed Forces Institute of Pathology,[23] random reports indicate predominance in males and an age range from the second through the sixth decade, with a mean age around 35 years. Trichofolliculomas have been found in both black and white patients.

The characteristic histologic pattern is that of a large dilated or cystic follicle within the upper dermis which may communicate with the skin surface (Figure 11). The epithelium of the keratinous cystic space usually exhibits a distinct granular cell layer and exfoliates loose lamellar keratin similar to the normal follicular infundibulum. Follicles or follicle-like structures with or without dermal papillas branch or radiate from the primary epithelium, sometimes arborizing to form secondary or tertiary units (Figure 12). Two-dimensional sections of these complicated three-dimensional structures often yield complex-appearing histologic patterns. When hair shafts are formed, they are projected centripetally to form the clinical hallmark—a tuft of hairs or a wisp of wooly keratin.[24] Well-formed sebaceous elements may be found in association with follicular induction.[23] Histologic diagnosis is not difficult when follicular induction is advanced and the typical configuration is present. An exception to this is the occasional example of trichofolliculoma showing very limited follicular induction. In these variants, stromal determinants are weak or absent. Such lesions may closely resemble dilated follicular infundibula with budding lobules of indifferent epithelium suggesting primary germ. Such tumors, depending on the plane of section, more closely resemble the so-called dilated pore. Other tumors may contain incompletely organized matrix cells with some inner-sheath cell differentiation. The stroma is moderately cellular and loosely organized into a somewhat lamellar perifollicular sheath similar to that found in the normal follicle. Histochemical findings in studies of paraffin sections have been consistent with findings in normal hair follicles.

The presence of a large central ectatic follicle, in continuity with the epidermis, located in the mid and upper dermis, all suggest origin from the epithelium of the preexisting follicular infundibulum. The solitary character of the tumor, negative family histories, and lack of association with other abnormalities suggest an acquired lesion without genetic overtones. There is no explanation for apparent topographic limitation of the

tumor to the head and neck, and the extent of the morphologic spectrum of trichofolliculomas with very limited or negligible stromal induction has not been defined.

Tumors of Hair Germ

Trichogenic Tumors

Trichogenic tumors are a very rare group of primary cutaneous neoplasms.[3,25] So few tumors have been recognized and carefully studied that a complete classification is not yet possible. Trichogenic tumors are, however, entirely analogous to the more common odontogenic tumors and can be similarly divided into two primary groups, epithelial and mesenchymal. Epithelial trichogenic tumors can be further subdivided into those which are purely epithelial, and into epithelial tumors with mesenchymal components which may or may not cause inductive change. Pure epithelial neoplasms are termed *trichoblastomas*. Mixed epithelial-mesenchymal neoplasms showing only the earliest phase of stromal induction are called *trichoblastic fibromas*. Mixed epithelial-mesenchymal tumors demonstrating complete hair follicle formation are termed *trichogenic trichoblastomas*. Mixed epithelial-mesenchymal tumors of the dermal papilla are obscure but probably occur (see trichogenic myxoma). The classification listed in Table 2 is tentative.

Most of the epithelial trichogenic tumors studied thus far have been sharply circumscribed masses greater than 1 cm in diameter occurring in the lower dermis or at the dermal–subcutaneous interface. None have been in continuity with the epidermis and none have been located on the scalp. The overlying epidermis is generally not significantly altered.

Trichoblastoma

Trichoblastomas are pure epithelial tumors of hair germ without evidence of inductive change. These tumors are not clinically distinctive.

Table 2—Classification of Trichogenic Tumors

Epithelial trichogenic tumors without inductive change
Trichoblastoma
Epithelial trichogenic tumors with inductive change
Trichoblastic fibroma
Trichogenic trichoblastoma
Mesenchymal trichogenic tumors
Trichogenic myxoma

Only two such tumors have been so classified by the author. Both appeared as discrete well-circumscribed nodules at the juncture of dermis and subcutis.

Microscopically, trichoblastomas are composed of lobules of small uniform basaloid cells with a prominent peripheral nuclear palisade. In one tumor, narrow interior clefts separated major lobules with immature-appearing epithelial buds arising from a lobular surface (Figure 13). There was no cellular pleomorphism.

Trichoblastic Fibromas

The trichoblastic fibroma is an epithelial trichogenic tumor in which there is a minimal inductive effect of the mesenchymal component. All tumors studied thus far have been sharply circumscribed nodules greater than 1 cm in diameter occurring at the junction of dermis and subcutis. A very large trichoblastic fibroma 8 cm in diameter weighing 259 g has been reported as a giant solitary trichoepithelioma.[26] None have been from the scalp.

Histologically, the trichoblastic fibroma consists of three-dimensionally complex lobular islands of cuboidal or low columnar epithelial cells embedded in a moderately cellular fibroblastic matrix (Figure 14). Division figures are rarely encountered. A distinctive epithelial feature is the formation of a primary germinal bud which recapitulates the primitive budding of primary hair germ from the embryonic periderm (Figure 15). Another distinctive feature is the formation of long thin strands of epithelial cells, usually only one or two cells thick, surrounded by a relatively dense hyalinized stroma. Such areas may represent a focally advanced inductive effect. Some epithelial islands include small keratinous cysts containing remnants of lamellar keratin. True hairs are not formed. Polarization microscopy reveals occasional tonofibrils within epithelial cells which become most prominent in areas of keratinization. The stroma is composed of loosely arranged fibroblastic cells separated by hyaluronidase-sensitive ground substance in the immediate paraepithelial zones. A somewhat storiform or lamellar pattern of stromal cells is occasionally noted. Sebaceous cell differentiation may occur.

Trichogenic Trichoblastoma

The trichogenic trichoblastoma is an epithelial trichogenic tumor in which focal stromal induction results in the development of organized hair follicles. Two such neoplasms have been studied in detail,[25] one from the buttock and one from the groin. Both appeared as sharply circumscribed pseudoencapsulated masses in the lower dermis or subcutis.

Histologically, the trichogenic trichoblastoma is formed by interconnecting tumor lobules. The peripheral margin of a lobule is composed of a stromal mantle which may appear quite dense and hyalinized. Stroma becomes more cellular and increases in hyaluronidase-sensitive ground substance adjacent to epithelium. The undifferentiated epithelial component consists of uniform basaloid cells which frequently line up in two cell columns with various branchings and bifurcations (Figure 16). Follicles in various stages of differentiation are found in continuity with epithelial cords (Figure 17). An unusual degree of topographic organization may be found, for when hairs are formed, there is a tendency for hair bulbs to be oriented to the periphery and for hairs to be projected towards the center of the lobule. Hairs originating from completely developed follicles are usually contained within epithelial sheaths until they project into small keratinous cysts. Focal sebaceous differentiation may be present.

The diagnosis of well-differentiated tumors is not difficult because of the presence of hairs. Large trichoepitheliomas may closely simulate trichoblastic fibromas, but trichoepitheliomas are generally not pseudoencapsulated and are intradermal. The primary germinal bud may be seen in the trichoepithelioma, but the distinctive narrow double cell epithelial column is usually absent. Trichoblastomas resemble basal cell carcinomas histologically and cytologically, but trichoblastomas are sharply circumscribed tumors which do not lie within the dermis and lack the associated mucinous stroma of basal cell carcinoma. Complex hamartomas of hair germ are found occasionally as a component of the nevus sebaceous complex. These may include inductive stromal elements and evolve some degree of follicular morphodifferentiation. True hair formation, however, has not yet been identified as a secondary phenomenon in the hamartomatous component of nevus sebaceous.

Although aggressive variants of some odontogenic analogs are well known, similar trichogenic neoplasms have not yet been identified. This may be purely a matter of recognition.

Trichogenic Myxoma

Trichogenic myxoma is an epithelial-mesenchymal trichogenic tumor which is probably best classified as a hamartoma of the dermal papilla.

Morphologic studies are based on several tumors removed from a single patient over a period of several years. Clinically, asymptomatic nondescript nodular masses 1 to 2 cm in diameter appeared at the junction of the dermis and subcutis. These were excised without recurrence.

Histologically, there may be a unique combination of nodular masses of

myxoid stroma rich in hyaluronic acid and small islands of squamous epithelium (Figures 18 and 19). Some small tumors are, in a single section, exclusively myxoid, somewhat resembling a true myxoma; others are more suggestive of a myxoid neurofibroma. One such myxoid tumor contained small cystic nodules resembling dermoid cysts with sebaceous cell differentiation. Small foci of heavily pigmented epithelium and stellate melanocytes are also found in some areas.

The trichogenic myxoma may be considered structurally and histogenetically analagous to the odontogenic myxoma. Although aggressive variants of the odontogenic myxoma are described, the trichogenic equivalent is not known.

Tumors of the Hair Matrix

Trichomatricoma

Trichomatricoma (pilomatricoma, calcifying epithelioma)[27,28] is a benign tumor of adnexal keratinocytes, in which there is limited cytodifferentiation toward cells of hair matrix, the hair cortex, and cells of inner sheath.

About 50% of all lesions are found on the head and neck, another 25% on the arms, with the remainder distributed over the trunk and lower extremities. No cases have been reported from the palms or soles. Characteristically a tumor of the young, 40% of trichomatricomas are biopsied before age 10, and 60% before age 20.[29] An association with Gardner's syndrome had been noted,[30,31] and a few examples of patients with multiple lesions have been reported.[32,33] Familial occurrence of trichomatricomas has also been noted, including multiple tumors in a patient with myotonic dystrophy[34] and in a patient with multiple tumors and hypercalcemia.[35] Familial occurrence and other associated abnormalities are very infrequent and are probably coincidental, with the possible exception of Gardner's syndrome.

Small and presumably early tumors are sharply circumscribed and cystlike, with a proliferative perimeter of uniform small dark cells closely resembling hair matrix cells. In the proliferative areas (Figure 20), nucleic acid synthesis has been demonstrated *in vitro*,[36] and division figures are frequently observed in histologic sections. With growth and maturation, tumors become multilobular, with irregular outlines (Figure 21). Matrix cell specialization may either be toward hair cortex with a formation of dense translucent hyaline substance closely resembling hard keratin or towards large squamoid keratinocytes with prominent keratohyaline granules suggestive of inner sheath cells. Necrobiosis of matrix cells produces

coherent masses and columns of highly distinctive anucleate shadow cells, while more complete necrosis will occasionally result in an area of acellular debris (Figure 22). Polariscopic examination reveals a characteristic pattern of coarse intracytoplasmic anisotropic fibrils in shadow cells. Properly organized hair shafts are never found. Dystrophic calcification of epithelium occurs frequently, and osseous metaplasia of stroma is occasionally found with formation of both lamellar and woven bone (Figure 23). Small amounts of melanin can be found in about 10 to 15% of trichomatricomas. Stromal amyloid has been found by conventional stains and by electron microscopy. Interlobular stroma is an inconspicuous element of trichomatricoma, and epithelial components are poorly vascularized. A brisk stromal foreign body reaction is frequently encountered, however, probably in response to keratin. Occasional tumors appear completely necrobiotic with no viable matrix cells remaining.

Minor histologic variants include tumors with abundant melanin [37] and tumors with extensive osseous metaplasia. Matrix cell differentiation undoubtedly occurs in other tumors which cannot be classified as trichomatricomas including trichogenic trichoblastomas, rare trichoblastic hamartomas with nevus sebaceous, and in other rare and as yet unclassified matrix cell neoplasms.

Cumulative histochemical evidence and electron microscopic studies broadly support the histogenetic postulate that trichomatricoma takes origin from or differentiates towards hair matrix cells. The most important histochemical findings are similarities in intensity and distribution of -SH and -SS groups between the sulfur-rich proteins of shadow cell precursors and normal cells of hair cortex.[28,38] A homologous pattern of distribution of citrulline is found in some areas of lamellar keratin and keratin of the inner sheath.[39] Ultrastructurally, most of the keratinizing cells of trichomatricoma contain filamentous α-keratin but not keratohyaline granules.[40] This pattern of keratinization in tumor cells is similar to that of the normal hair cortex but is unlike that of the epidermis.

Nosologically, trichomatricoma is best considered as a hamartoma of the hair follicle. It is possible that, during cyclic renewal of the hair follicle, normal follicular histogenesis is incomplete following an arrest or other abnormality of stromal induction during anagen. Presumptive matrix then fails to organize normally and although some limited cytodifferentiation occurs, morphodifferentiation does not. In the absence of adequate stromal induction, well-formed hair shafts are never seen. It is probably significant that a rich blood supply for the matrical epithelium does not develop. The final result is undoubtedly a benign tumor of very limited growth which ultimately will undergo spontaneous involution, a

characteristic shared with few other neoplasms but consistent with a genetically programmed short life-span for the matrix cells. It may be that the duration of growth of matrix cells of the trichomatricoma is approximately the same as the normal anagen time of the follicle from which it was derived.

A single example of a nonmetastasizing cytologically atypical and histologically aggressive matrix cell tumor has been described.[41] Although exotically rare, the occurrence of trichomatrical carcinoma must be considered possible.

Tumors of External Hair Sheath

Tricholemmal Cysts

Tricholemmal cysts, or common wens, for many years have been inappropriately referred to as "sebaceous cysts." Synonyms include pilar cyst and trichochlamydo cyst. Their occurrence is often familial, with inheritance as an autosomal dominant trait. Clinically, they appear as single or multiple, firm intradermal or subcutaneous nodules distributed predominantly on the scalp (90%) but with a few found on the face, trunk, and extremities.[42] They are not found on glabrous skin. Tricholemmal cysts are often clinically distinguishable from epidermoid cysts: the tricholemmal cyst, unlike the epidermoid cyst, often has a distinctive cutaneous punctum. It is also characteristic for the tricholemmal cyst to shell out easily from the skin while the epidermoid cyst is tenaciously adherent to the surrounding stroma (Figure 24).

The microscopic hallmark of the tricholemmal cyst is a mode of keratinization which simulates the inner zone of the normal outer hair sheath between the bulge and the entrance of the sebaceous duct. In cyst epithelium, there is an abrupt transition from nucleated luminal cells to dense lamellar keratin, usually without the formation of keratohyaline granules or the presence of a granular cell layer. The basal or germinative layer of the cyst is often distinctly palisaded and is aligned to a prominent basement membrane similar to the hyaline membrane of the outer sheath. These histologic features readily distinguish tricholemmal cysts from epidermoid and dermoid cysts of the skin (Figure 25).

Polariscopic examination adds another useful dimension to routine light microscopy for the intracellular pattern of birefringent tonofibrils is both distinctive for the tricholemmal cysts and different from the pattern encountered in the epidermoid cyst. In the epithelium of the tricholemmal cyst, tonofibrils are aggregated into coarse sheaves and remain more or less perpendicularly oriented as they do in the normal follicular isth-

mus, while in the epidermal mode of keratinization the more delicate tonofibrils usually become horizontally oriented in the upper Malpighian layer.

The vascular supply is composed of small vessels distributed in the stromal adventitia of the cyst. Only rarely do vessels invaginate cyst epithelium. Foci of dystrophic calcification are common. Granulomatous transformation of the cyst lining may be seen, but this is less common than in epidermoid cysts. Marsupialization is occasionally found.

The soft pultaceous character of the cyst contents from the freshly removed cyst is probably a result of complete hydration and partial enzymatic decomposition of the exfoliated keratin. Enzyme histochemical studies of cyst epithelium demonstrate abundant hydrolytic enzymes which although concentrated in the zone of keratinous transformation apparently diffuse into the keratin itself. Strong epithelial reactions for oxidative enzymes are also found.

Melanocytes have not yet been found in the epithelium of tricholemmal cysts, although nonbasal ATPase-positive dendritic cells can be demonstrated. The ultrastructural features of keratinization in tricholemmal cysts are different from epidermoid cysts.[42]

The proliferative areas occasionally encountered in tricholemmal cysts usually cause little interpretive difficulty. Examples may be encountered, however, which are in a morphologic continuum with the proliferating tricholemmal tumor. Such proliferative cysts have been undoubtedly interpreted in the past as carcinomatous change in so-called sebaceous cysts. The reported incidence of 1 to 2% [43,44] malignant transformation is undoubtedly too high, as a critical review of these studies suggests a poorly documented heterogeneous group of cystic lesions as judged by contemporary standards and terminology. If proliferating tricholemmal tumors be considered separately, malignant transformation of keratinous cysts must be considered very rare.

Proliferating Tricholemmal Tumors

Proliferating tricholemmal tumors are uncommon neoplasms of outer sheath cells which often result in a distinctive clinicopathologic picture. Frequently quite large (up to 25.0 cm) and exophytic, these neoplasms are confined almost exclusively to the scalp and back of the neck. They are approximately five times more common in women. While the age range of subjects is from the fourth to the ninth decade, the mean age is about 65 years. Prolonged duration is characteristic. The usual clinical diagnosis is squamous cell carcinoma.

The histologic features, although variable among different tumors, are

nevertheless sufficiently distinctive to be diagnostic. These include: a) a sharply circumscribed pattern of convoluted lobules with pushing margins; b) frequent continuity with the epidermis; c) extensive areas of tumor cell necrosis; d) tricholemmal type keratinization with abrupt transition to dense keratin but without formation of a granular layer (Figures 26 and 27).

Reserve cell differentiation is generally toward large polygonal keratinocytes. Basal or reserve cell orientation to a prominent hyaline PAS-positive basement membrane is occasionally found but is not a constant feature.

There is some loose perilobular stroma but poor vascularization. Occasional stromal foreign body reactions are encountered similar to that seen in trichomatricomas. Polarization microscopy is characteristic; in those tumors with peripheral epithelial cell organization similar to that found in the tricholemmal cysts, prominent tonofibrils are oriented vertically to the epithelial–keratinous interface. Throughout the epithelial lobules the anisotropic tonofilamentous pattern exhibits individual cell keratinization without formation of lamellar keratin. In some tumors, extensive areas of tumor cell necrosis are found with formation of amorphous keratin debris.

Cytologic variants include clear-cell types suggestive of giant tricholemmomas and dyskeratotic forms suggestive of adenoid squamous cell carcinoma. The lobular growth pattern and tendency for centripetal keratinization of large trichomatricomas can simulate proliferating tricholemmal tumors, but the former can be differentiated by recognition of matrix cells and by polarization microscopy (viable matrix cells contain no or few anisotropic tonofibrils).

Histologic patterns of aggressive growth are occasionally present, and as mentioned, cytologic atypism may be encountered. Of 31 patients accumulated from four recent studies, only one experienced a solitary regional node metastasis, and death from disseminated neoplasm has not been reported. There is every indication that a microscopic diagnosis of carcinoma in such a neoplasm should be made with restraint.

Terminology has been confused and histogenesis uncertain. These tumors were first grouped as an entity under the term *proliferating epidermoid cysts.*[45] Almost simultaneously, a separate study independently described this neoplasm as invasive pilomatrixoma.[46] An additional series was subsequently reported as trichochylamydocarcinoma [47] in which origin was believed to occur from the lower external sheath. A more recent report of giant hair matrix tumor [48] reaffirmed matrical origin. Proliferating epithelial foci are not exceptional in tricholemmal cysts, and several small cystic tumors of a type intermediate between tricholemmal

cysts and fully developed proliferating tricholemmal tumors have been seen by the author. A key factor in proliferation may be vascularization of the cyst epithelium possibly secondary to focal injury. Until additional histochemical and ultrastructural details are known, histogenesis will be in some doubt, although the weight of contemporary evidence strongly favors hair sheath origin. Proliferating tricholemmal tumor is nosologically the best term. The malignant variant should be termed malignant proliferating tricholemmal tumor in distinction to tricholemmal carcinoma, which is the malignant form of tricholemmoma.

Tricholemmal Keratosis

Tricholemmal keratosis is a rare keratinizing tumor which resembles a cutaneous horn or hyperkeratotic actinic keratosis (Figure 28). Too few examples have been studied to provide meaningful clinical data.

Histologically, there is striking orthokeratotic hyperkeratosis and verrucous hyperplasia of epidermis but without the formation of a granular cell layer. At the epidermis there is abrupt transition between the epidermal and tricholemmal mode of keratinization. The pattern of keratinization within the keratosis is similar to that seen within the normal follicular isthmus or within the tricholemmal cyst in which large pale keratinocytes abruptly transform into dense sheets of lamellar keratin (Figure 29). In the subepidermal zone there are contiguous epithelial lobules of large palestaining keratinocytes. The periphery of the lobule is characterized by a margination of basal cells. Centripetal keratinization of lobules is in the same manner as that of the tricholemmal cysts (Figure 29). A few secondary germinal buds are found proliferating from peripheral lobular epithelium. Tumor lobules in the deeper portion of the dermis closely simulate those seen in proliferating tricholemmal tumors. It is not clear whether this lesion is actually a tumor of the hair follicle or represents a phenotypic change in the epidermal and infundibular keratinocyte. The mode of keratinization, however, is unequivocally tricholemmal.

Tricholemmoma

Tricholemmoma [3,49,50] is a benign neoplasm of hair follicle which is derived from or differentiates towards cells of the outer sheath. Clinically nondescript, these small tumors (usually less than 1 cm) are typically present on the face. The most common clinical diagnosis is basal cell carcinoma. Age at the time of diagnosis ranges widely from the third to the ninth decades.

Histologically, the tricholemmoma is a sharply circumscribed lobulated epithelial neoplasm usually in continuity with the epidermis or with follicular epithelium at several points (Figure 30). The deep dermis is

rarely involved. Peripheral reserve cells of the lobule tend to palisade and are associated with a prominent basement membrane reminiscent of the vitreous sheath of the normal follicle (Figure 31). Large lobules may have small keratinous microcysts containing lamellar keratin. The nonlobular variants as noted by Lever [51] are properly follicular hamartomas and should not be classified as tricholemmomas.

A cytologic hallmark of the tricholemmoma is some degree of cytoplasmic glycogenosis which in paraffin sections produces a "clear cell" neoplasm. Glycogen content decreases in zones of transition between tumor lobules and follicular epithelium or epidermis. Cells in transitional areas appear as intermediates between epidermal or infundibular keratinocytes and the water clear cell of the outer sheath. Small squamous eddies may be found occasionally in transitional areas. Individual tumor cells are smaller than the epidermal keratinocyte, are vaguely polygonal in outline, and have small somewhat homogeneous nuclei with small but distinct nucleoli. Clear cells contain abundant glycogen (Figure 32). Anisotropic tonofibrils are found in intermediate or transitional cells. Enzyme histochemical and electron microscopic studies have not been reported.

In large tricholemmomas where clear cells predominate, the most troublesome differential diagnosis is the clear cell variant of eccrine acrospiroma (clear cell hidradenoma). The lobular growth pattern and focal epidermal continuity of acrospiroma may simulate tricholemmoma, but the acrospiroma does not display a peripheral cellular palisade or a prominent glassy basement membrane. The reserve cell of the acrospiroma is adjacent to the stromal vessels and is not always at the periphery of the lobule. In small lesions, where intermediate cells may predominate, differentiation from the so-called irritated seborrheic keratosis (inverted follicular keratosis) may be difficult. Occasionally, a small palisading basal cell carcinoma may have areas of clear cells due to accumulation of lipid or glycogen and can also be mistaken for small tricholemmomas.

The tricholemmal carcinoma is a histologically invasive, cytologically atypical clear cell neoplasm of adnexal keratinocytes which is in continuity with the epidermis and/or follicular epithelium (Figure 33). Metastasizing examples have not been reported. Tricholemmal carcinoma is not synonymous with malignant proliferating tricholemmal tumor.

Tumors of Perifollicular Mesenchyme

Trichodiscoma

The hair disc (haarscheibe) is a slow-adapting mechanoreceptor found in animal skin which consists of a highly vascularized thickening of the

papillary dermis covered by epidermis containing Merkel cells. Myelinated nerves terminate at the dermal–epidermal interface and within the dermal pad. Similar structures have been tentatively identified in human skin.

In 3 patients described,[52] hundreds of small skin-colored papules were widely distributed. Onset of lesions was variable, and individual lesions were persistent but did not increase in size beyond 1 to 3 mm. There were no associated symptoms and no reported systemic abnormalities.

Histologically, individual lesions are expansile sessile nodules in the papillary dermis composed of loosely aggregated collagenous and elastic fibers in a hyaluronidase-sensitive mucinous matrix. Small blood vessels may be prominent, and stellate stromal cells containing argyrophilic granules consistent with melanin have been noted. Prominent myelinated nerves and hair follicles may be found in proximity.

The histologic differential diagnosis includes papular mucinosis and perifollicular fibromas. The former can be differentiated on clinical grounds. Separation from perifollicular fibroma may be more difficult. A case having features of both trichodiscoma and perifollicular fibroma has been described.[52]

Perifollicular Fibromas

The common denominator of the few reports of lesions, collectively termed *perifollicular fibromas*,[53–55] has been lamellar fibroplasia of the peritrichium (perifollicular stroma).

Clinically, perifollicular fibromas have been asymptomatic single or multiple skin-colored lesions of the head and neck varying from 1 to 5 mm in size. Familial examples have not been reported.

Histologically, there is concentric hyperplasia of the peritrichium of small vellus hair follicles. Hyaluronidase-sensitive mucosubstances are increased in the perifollicular zone. Inflammation is usually inconspicuous.

A congenital lesion designated as a perifollicular fibroma [58] would be equally consistent with a solitary hamartoma of hair germ. If there is a prominent capillary vascular component and associated nerves, trichodiscoma becomes a consideration.

Most of the tumors reported as perifollicular fibromas have been acquired. There is a good possibility that some of these lesions represent an exaggerated response to inflammation or irritation and are therefore reactive. Minor degrees of peritrichial fibroplasia, particularly on the nose, are commonplace in biopsies done for other purposes.

Pilar Leiomyoma

Although there is little factual data, it is generally believed that some of the multiple and most of the solitary nondartoic leiomyomas of skin arise from arrector pili muscles.[56] Clinically nodular or plaque-like, leiomyomas microscopically present irregular extensions into adjacent dermis. On occasion, proliferating muscle cells may be interspersed with considerable fine collagen, making positive recognition difficult even with the aid of differential stains. Bizarre cytologic variants similar to those seen in the gastrointestinal smooth muscle and uterus have not yet been described in skin. Occurrence in families and in twins [56,57] has suggested a hamartomatous condition in some instances, possibly inherited as an autosomal dominant trait with incomplete penetrance. Primary leiomyosarcomas of skin capable of metastasis are very rare neoplasms.

Tumors of the Intraepidermal Follicle and Infundibulum

Inverted follicular keratosis

Inverted follicular keratosis [59,60] is a small, benign keratosis largely limited to the head and neck with predilection for the upper lip and cheek. Although widely accepted as a histologic entity, there is a paucity of clinical information including age and sex distribution and natural history. Individual lesions are small, solitary, frequently elevated, and occasionally exophytic. Verruca vulgaris is a common clinical diagnosis.

Histologically, the inverted follicular keratosis is characterized by sharply circumscribed digitiform, lobular, or pyriform masses of keratinocytes in continuity with epidermis or follicular epithelium but invaginating into the upper reticular dermis. Within lobules, reserve cells are basal like, but there is a tendency for central-lobular squamous cell differentiation with the formation of distinctive squamous eddies; this feature is often emphasized as characteristic for this tumor. Hyperkeratosis is usually present and intraepithelial crypts are often keratin filled. There is negligible cytologic atypism.

When both the location and histologic findings are prototypical, the microscopic interpretation is not difficult. In practice, however, the following differential diagnoses often obtain: a) "irritated" seborrheic keratosis; b) verruca vulgaris, involuting; c) keratoachanthoma; d) tricholemmoma; e) benign keratosis. With attention to detail and the help of step or serial sections, most of the atypical cases can be resolved, except for that of seborrheic keratosis with squamous change.

The histogenesis of the inverted follicular keratosis (acrotrichoma)[61] is

thought to be from the follicular infundibulum. Most of the evidence in favor of infundibular origin is based on tumors first designated as inverted follicular keratosis and then shown to be in continuity with the infundibular zone. There are no unique histochemical or ultrastructural features. Moreover, squamous eddies in seborrheic keratosis, whether or not "irritated," result in nearly identical histologic patterns. Differentiation from seborrheic keratosis can be made on occasion, but only if one accepts the observation that seborrheic keratosis is always superficial. The current terminology might well be different if the original concept had been that of "inverted" seborrheic keratosis.

Tumor of Follicular Infundibulum

The tumor of follicular infundibulum [62,63] is a fenestrated sheet-like subepidermal proliferation of benign squamous epithelium in continuity with both epidermis and the upper outer hair sheath. Similar topographically to the multiple superficial basal cell hamartomas with focal follicular differentiation, tumors of follicular infundibulum characteristically have been single lesions without follicular differentiation.

Dilated Pore

The dilated pore [64] is clinically and histologically a comedo-like structure opening to the skin surface with apparent origin from follicular infundibulum including the follicular pore. The keratinizing wall is often somewhat hyperplastic but is not pseudoepitheliomatous.

Tumors of Miscellaneous Type

Trichoadenoma

A single case report [16] described a nodular intraepidermal aggregate of small, discrete cysts lined by epithelium resembling outer sheath cells with minimal central keratinization. None have been reported subsequently. Trichoadenoma is probably best considered a morphologic variant of trichoepithelioma (see trichoepithelioma).

Trichoma

In a morphologic study of basal cell tumors,[65] it was suggested that this term replace basal cell carcinoma (epithelioma), supporting the earlier view of Mallory that these tumors arise from hair matrix or hair "anlage" rather than epidermis.

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Legends for Figures

Figure 1—Congenital vellus hamartoma. Tangentially placed, closely packed normal vellus follicles form a small protruberant nodule. (H&E, × 16)

Figure 2—Congenital vellus hamartoma. Normal anagen vellus follicles are found at various levels in cross section. Hairs are normal. Eccrine ducts are not equally numerous. Nomarsky optics. (H&E, × 260)

Figure 3—Trichoblastic hamartoma. Arising in continuity with a nevus sebaceous, a pedunculated nodule containing many large and small epithelial islands extends from the scalp surface. (H&E, × 18).

Figure 4—Trichoblastic hamartoma. A ball of hair matrix cells arises in continuity with less specialized epithelium which forms a peripheral palisade. A distinctive double layered strand of epithelial cells extends from matrix cells to a large lobule. The adjacent stroma is cellular and loosely organized. Other epithelium contains melanin granules. (H&E, × 260)

Figure 5—Trichoepithelioma. A compact circumscribed stromal-epithelial proliferation produces an expansile intradermal nodule. Keratinous microcysts are present. (H&E, × 16)

Figure 6—Trichoepithelioma. A cellular fibroblastic stroma invests keratinous microcysts as well as masses of uniform undifferentiated epithelial cells. (H&E, × 260)

Figure 7—Trichoepithelioma (Trichoadenoma variant). Keratinous microcysts of similar size are closely grouped to form on intradermal nodule. Dermal collagen forms a dense stromal interstitium. (H&E, × 16)

Figure 8—Trichoepithelioma (trichoadenoma variant). The mode of keratinization within microcysts is epidermal—a thin granular cell layer gives way to loosely aggregated keratin lamillae. Note follicle-like structure. (H&E, × 162)

Figure 9—Trichoepithelioma. Delicately reticulated islands of basoloid epithelium are sharply circumscribed within a cellular fibroblastic stroma. In frequent contrast to basal cell carcinoma, stroma is not myxoid and there is no inflammation. (H&E, × 16)

Figure 10—Trichoepithelioma. A single field may closely resemble basal cell carcinoma. In trichoepithelioma epithelial mucin formation is less, there are very few division figures, and individual tumor cell necrosis is rare. (H&E, × 260)

Figure 11—Trichofolliculoma. Small follicular structures of vellus size bud in a radial array from a cystically dilated follicular infundibulum. Continuity with epidermis is invariable. (H&E, × 64)

Figure 12—Trichofolliculoma. Follicular epithelium is invested with a stroma similar to the peritrichium. When dermal papillas are formed varying follicular morphogenesis occurs. In the large central follicle matrix cells form trichokeratin but not a hair. (H&E. × 260)

Figure 13—Trichoblastoma. Individual tumor lobules are somewhat adamantinoid. A distinctive peripheral palisade of columnar nuclei appear contained within a basement membrane. A prominent basal vacuole results in apical displacement of peripheral nuclei. Tumor stroma is limited to delicate fibrous septa. (H&E, × 260)

Figure 14—Trichoblastic fibroma. This sharply circumscribed nodule 1.8 × 1.2 cm was "shelled-out" of the subcutis. The histologic pattern is small epithelial islands randomly distributed within a pale stromal matrix. (H&E, × 4)

Figure 15—Trichoblastic fibroma. A follicular or germinal bud extends from intranastomosing cords of epithelial cells. Note the typical fibrocellular stroma. The distinctive germinal bud recapitulates the primary follicular bud from embryonic periderm. (H&E, × 260)

Figure 16—Trichogenic trichoblastoma. Tumor lobules are sharply separated from adjacent subcutis. The cellular stroma increases in density in the paraepithelial zones. Delicate strands of intraanastomosing epithelium are characteristic. (H&E, × 120)

Figure 17—Trichogenic trichoblastoma. Note outer sheath transformation and mass of trichokeratin in an abortive follicle. Epithelial strands in continuity with the follicle are surrounded by a cellular stroma with abundant acid mucosubstances. Well-formed hairs were found in other sections. (H&E, × 250)

Figure 18—Trichogenic myxoma. A subcutaneous nodule is composed of an unusual array of dark-staining epithelial strands within a highly myxomatous stroma. The cavity contained an acellular pool of liquid mucin. (H&E, × 16)

Figure 19—Trichogenic myxoma. Well-differentiated epithelium is composed of non-keratinizing tonofilamentous keratinocytes. Mucins are of stromal origin. Nomarsky optics. (H&E, × 162)

Figure 20—Trichomatricoma (pilomatricoma). A large somewhat lobulated tumor 1.5 cm in diameter contains a few viable epithelial foci toward the periphery. Trichomatricoma is usually sharply separate from adjacent dermis and subcutis. (H&E. × 8)

Figure 21—Trichomatricoma (pilomatricoma). A small mass of proliferating dark staining matrix cells with central necrosis forms a small tumor in miniature. Large tumors are aggregates of such proliferative foci and their degenerative elements. (H&E. × 162)

Figure 22—Trichomatricoma (pilomatricoma). Matrix cells (*top*) may differentiate to form large pale staining keratinocytes (*center*) or undergo progressive necrobiosis to form parakeratotic foci (*right*) or distinctive anucleate shadow cells (*left*). (H&E. × 260)

Figure 23—Trichomatricoma (pilomatricoma). Occasional stromal metaplasia results in formation of lamellar bone. Note shadow cells. Nomarsky optics. (H&E. × 260)

Figure 24—Tricholemmal cyst. A small cyst is expanding into the subcutis. Note characteristic absence of investing stroma. Dark granular deposits of calcium salts are frequent. Keratin is characteristically dense and lamellar. (H&E. × 4)

Figure 25—Tricholemmal cyst. There is a peripheral palisade of reserve cells. Cells increase in volume as they proliferate but usually remain vertically oriented and do not develop a granular layer. Keratinization is abrupt. Nomarsky optics. (H&E. × 16)

Figure 26—Proliferating tricholemmal tumor. A large multilobular tumor 3.0 × 2.5 cm fills the dermis. Lobules with a distinctive folded or pleated pattern are characteristic. (H&E. × 4)

Figure 27—Proliferating tricholemmal tumor. The basal cell layer marks the proliferative zone of the tumor. Mature keratinocytes are shed directly into the adjacent stroma (*top*), appearing as small uniform hyaline bodies, but usually they do not evoke an inflammatory or giant cell reaction. (H&E. × 162)

Figure 28—Tricholemmal keratosis. Dense adherent keratin extends for more than 1 cm above the epidermal surface. An unusual pattern of epithelial lobules extends into the upper dermis. (H&E. × 16)

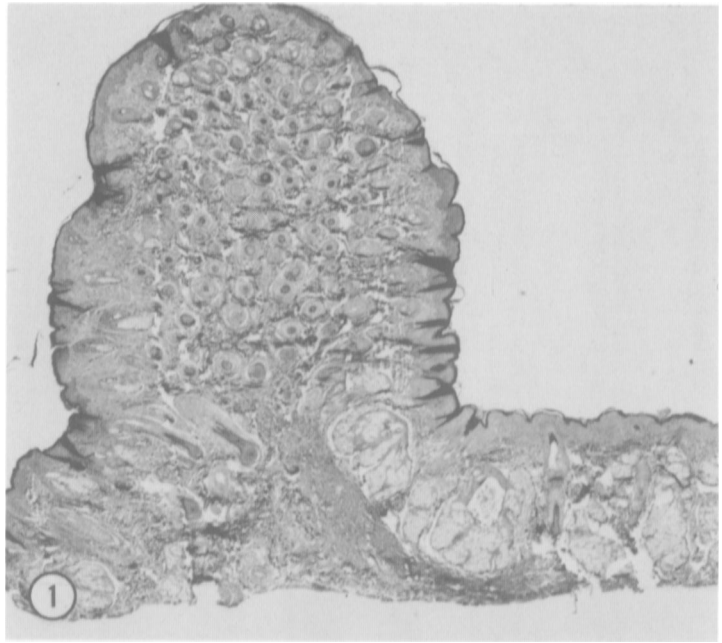
Figure 29—Tricholemmal keratosis. Lobules form central masses of keratin without formation of an intervening granular layer **(left).** The tricholemmal mode of keratinization at the epidermal surface is apparent **(right).** (H&E. **left,** × 162: **right** × 260)

Figure 30—Tricholemmoma. A sharply circumscribed nodular tumor is in continuity with the epidermis. Two small keratinous microcysts are present near the base. (H&E. × 16)

Figure 31—Tricholemmoma. Compact lobules with little intervening stroma form the bulk of the tumor. Lobules have a distinctive peripheral nuclear palisade and a prominent basement membrane. Clear cell glycogenosis is characteristic but is not uniformly present. (H&E. × 162)

Figure 32—Tricholemmona. Individual cells have distinct borders. Many in this field contain abundant cytoplasmic glycogen with displacement of a dense nucleus to one side of the cell. Division figures are rare. (H&E. × 406)

Figure 33—Tricholemmal carcinoma. A lobulated pale cell neoplasm is in continuity with the epidermis. Histologically similar to tricholemmoma, it is cytologically malignant. Nuclei are folded, chromatin is clumped, and division figures are frequent. Compare with tricholemmoma photographed at the same magnification (Figure 33). (H&E. × 406)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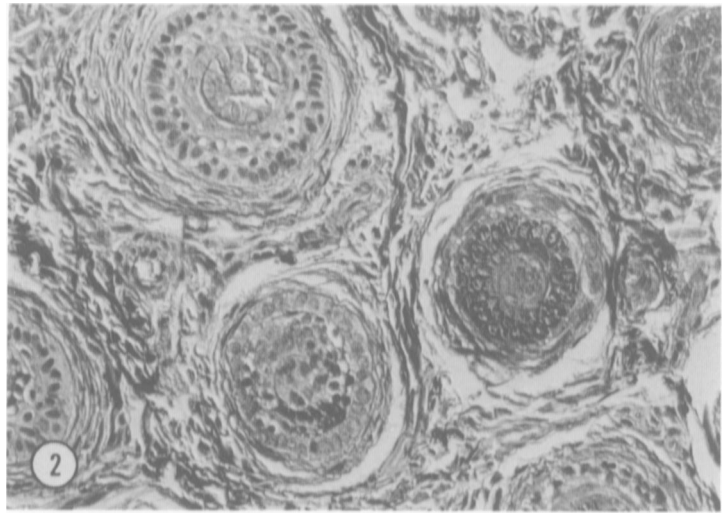
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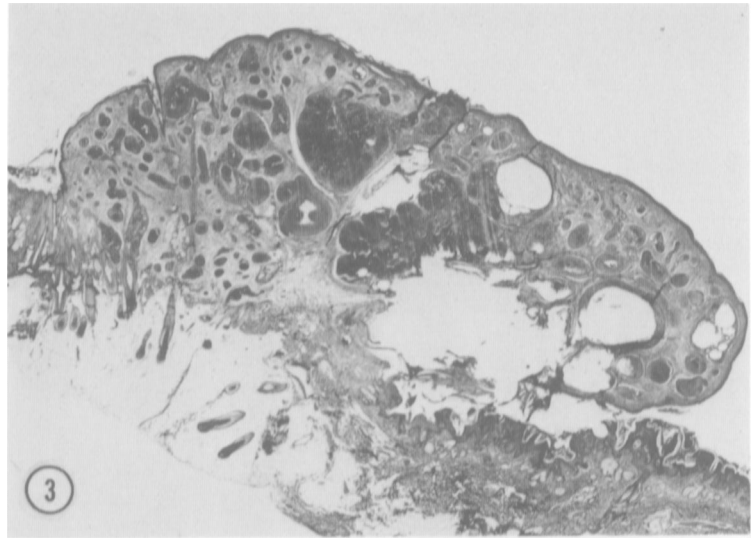
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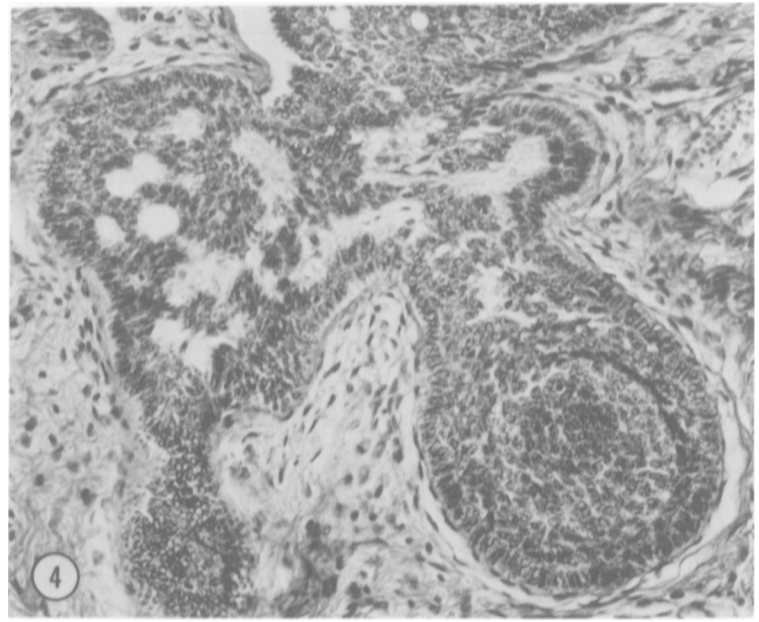
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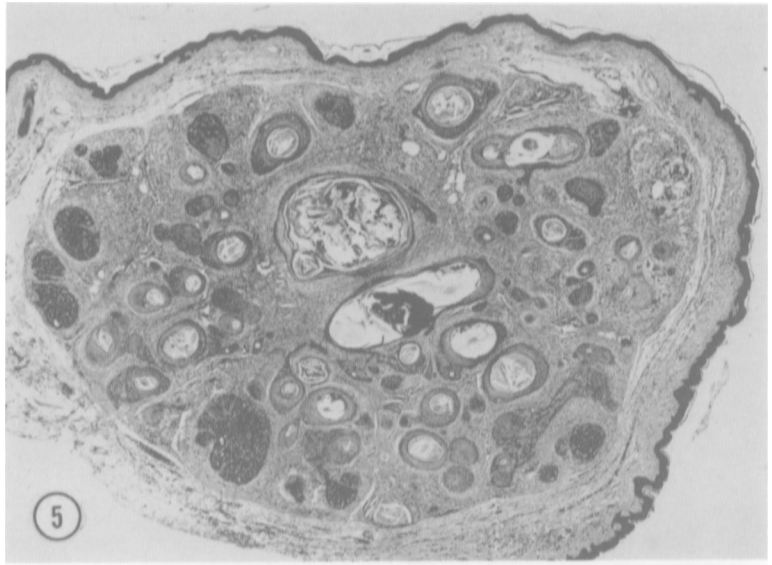
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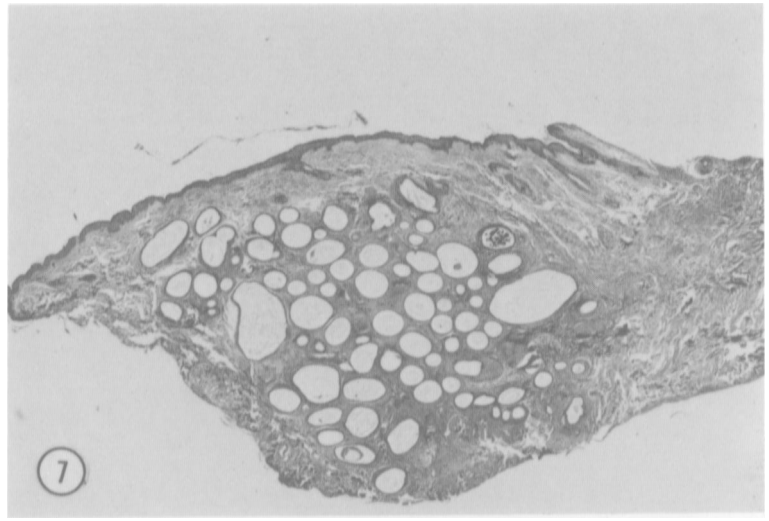
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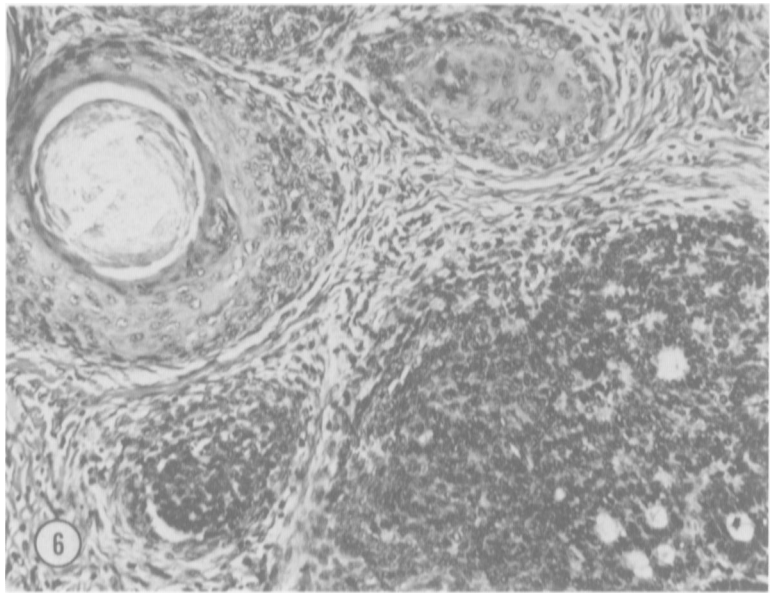
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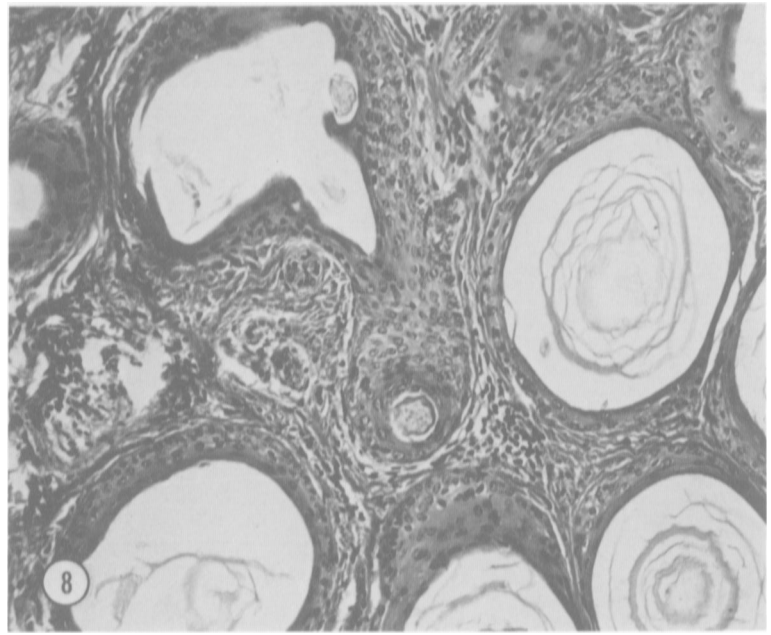
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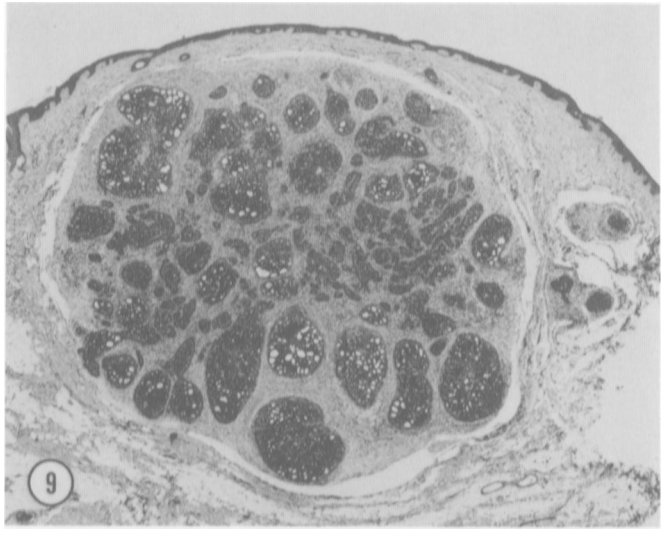
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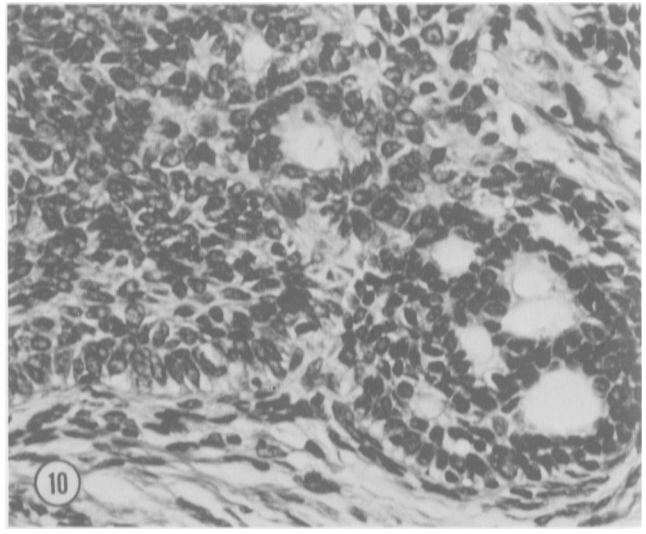
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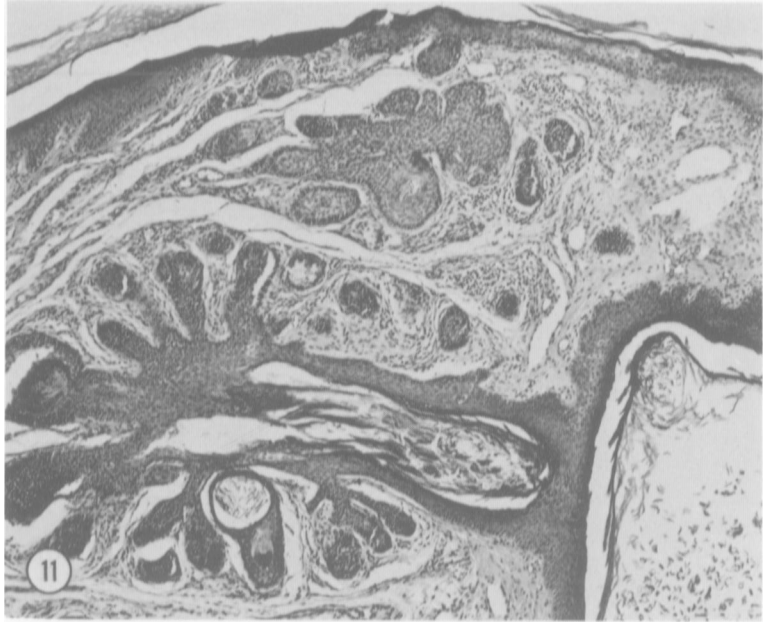
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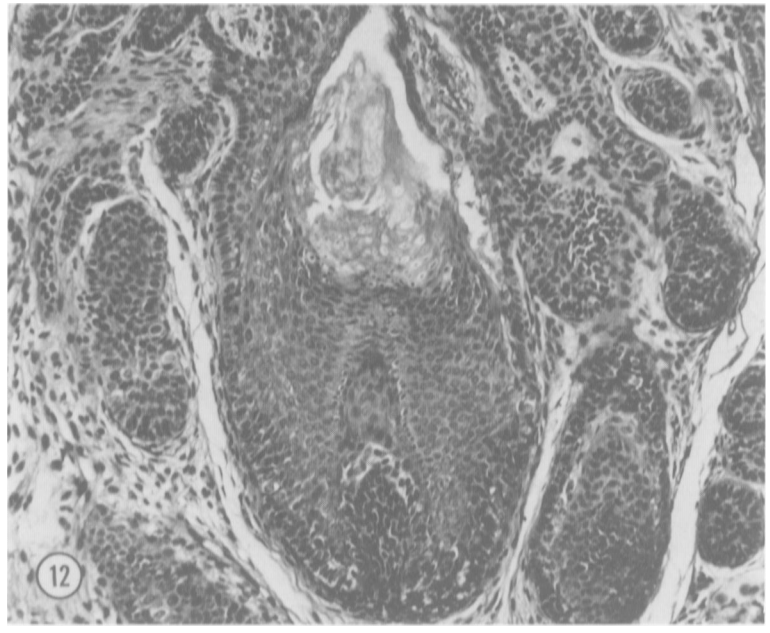
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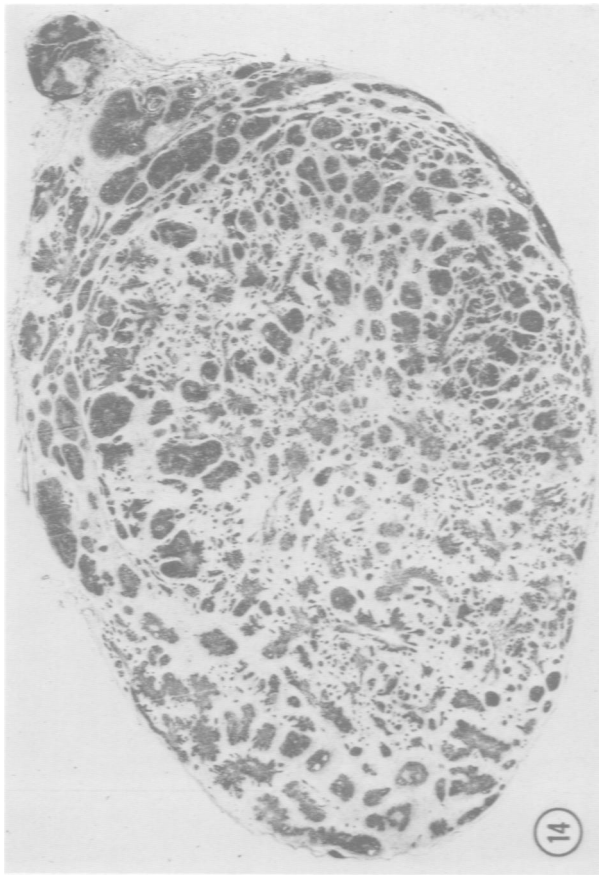

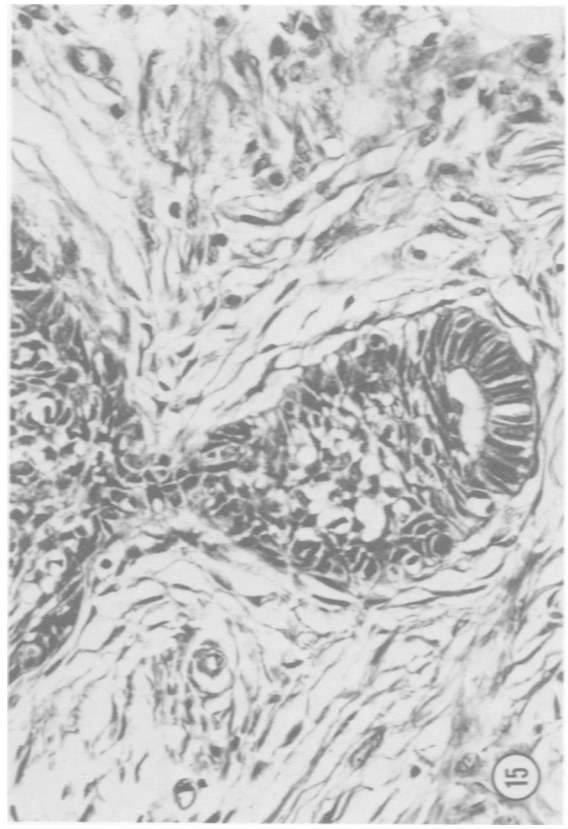

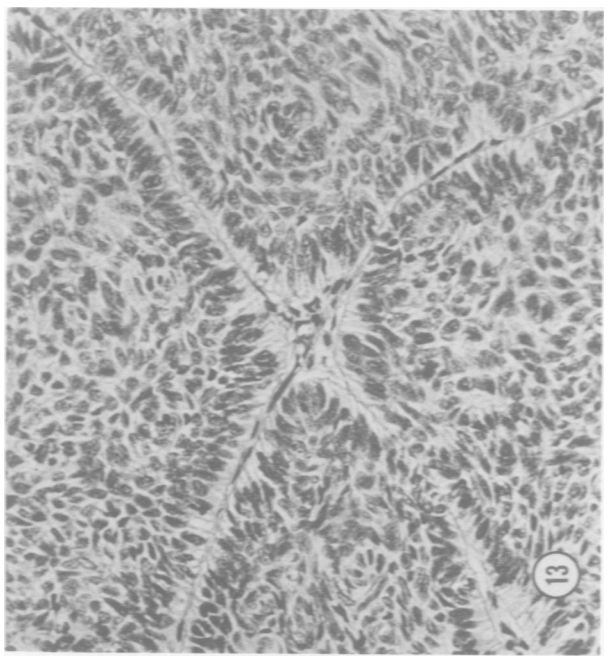

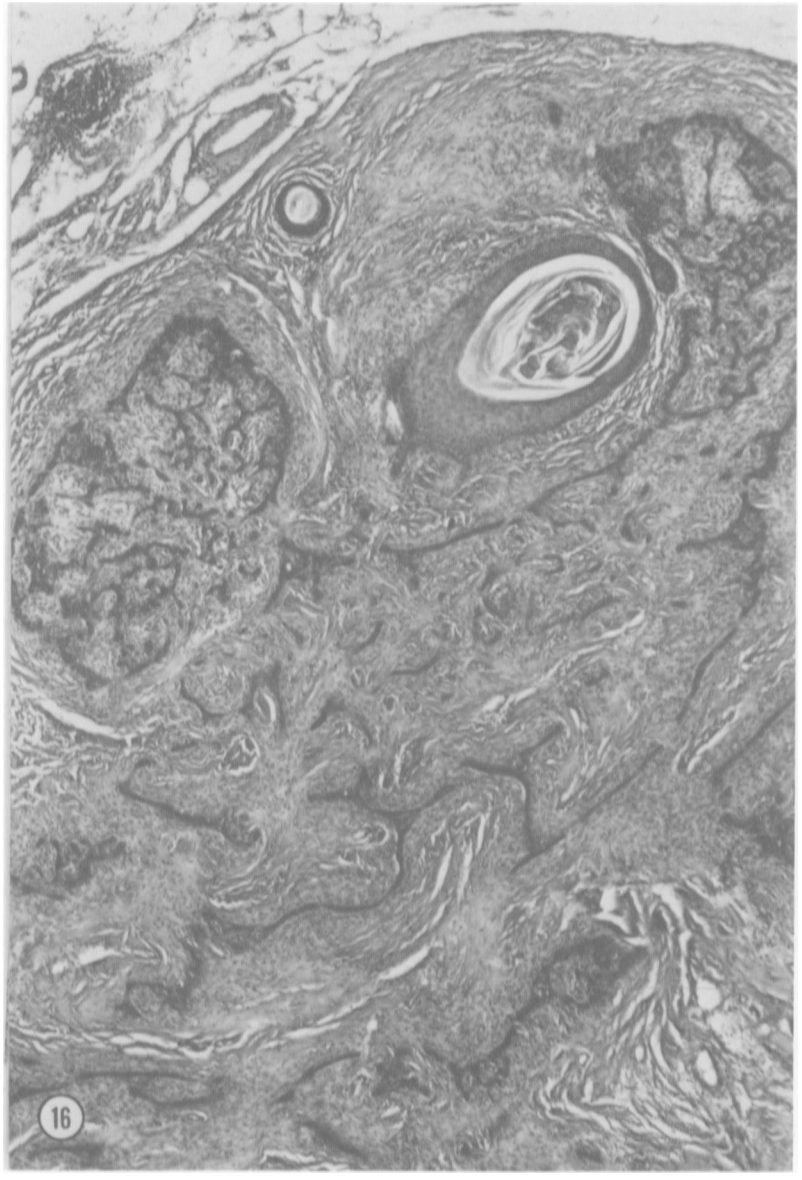
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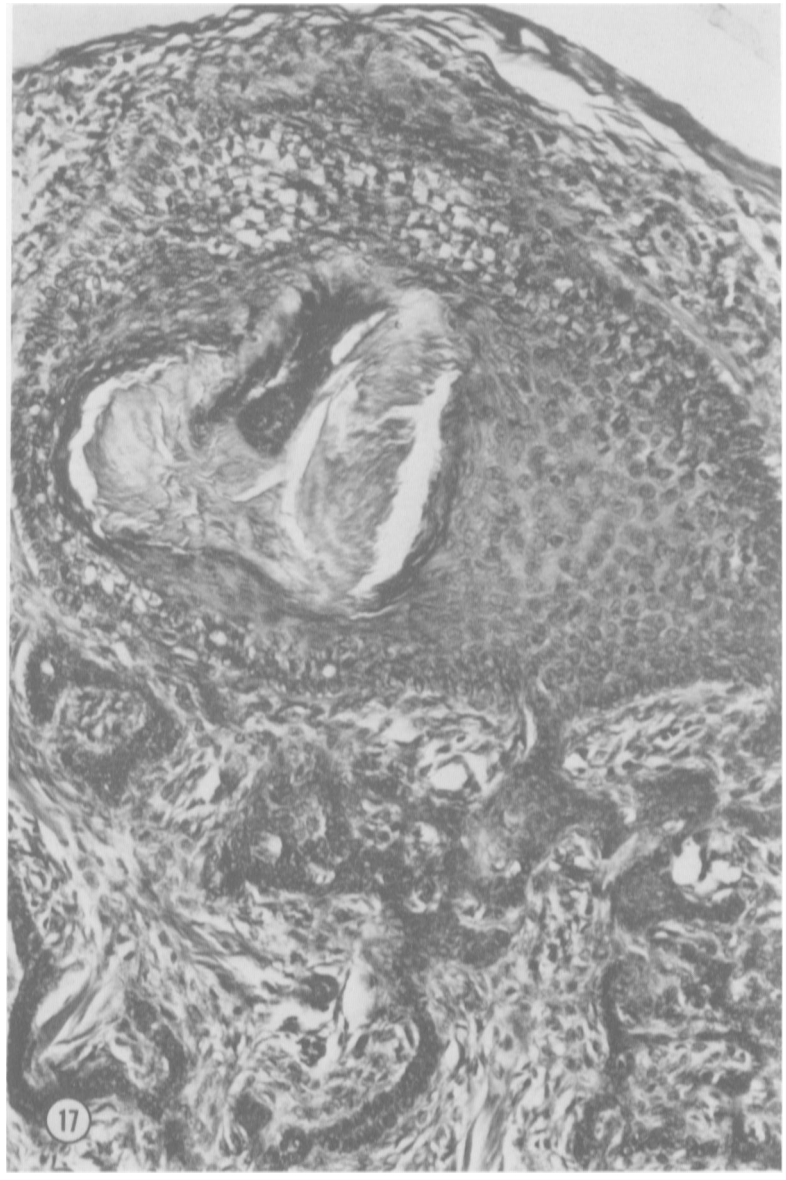
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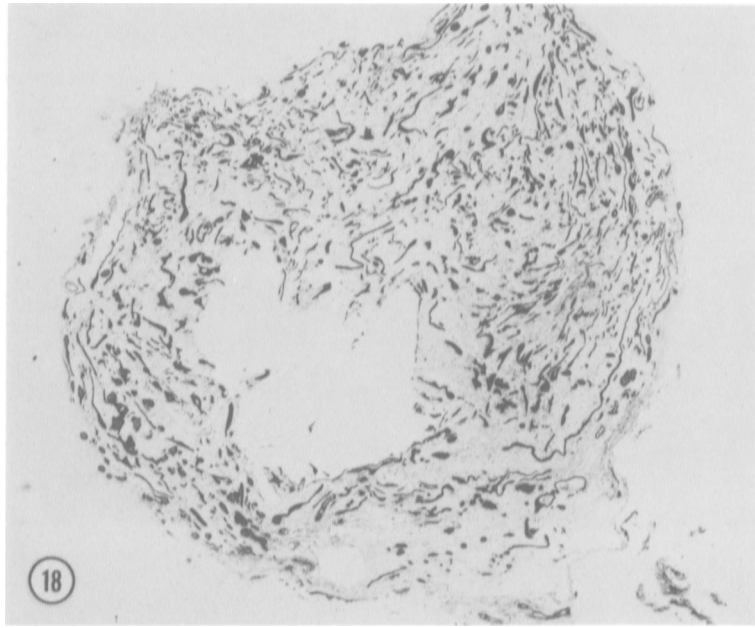
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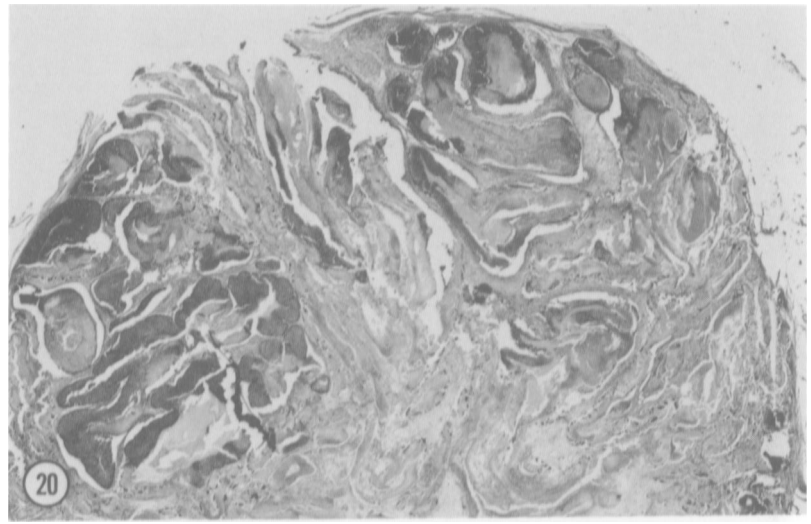
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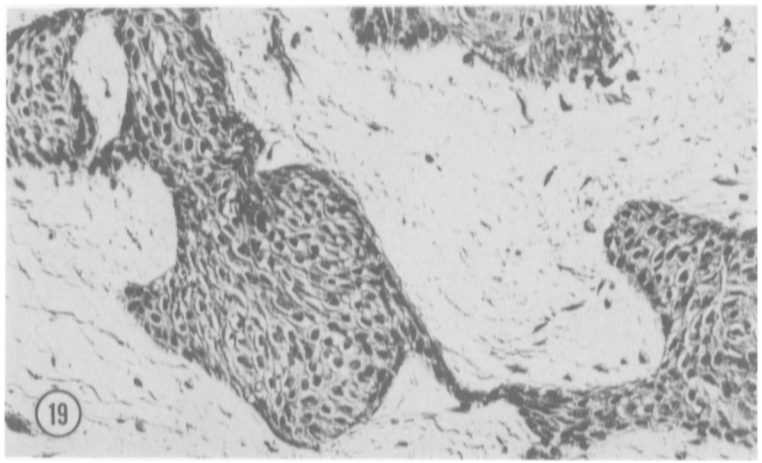
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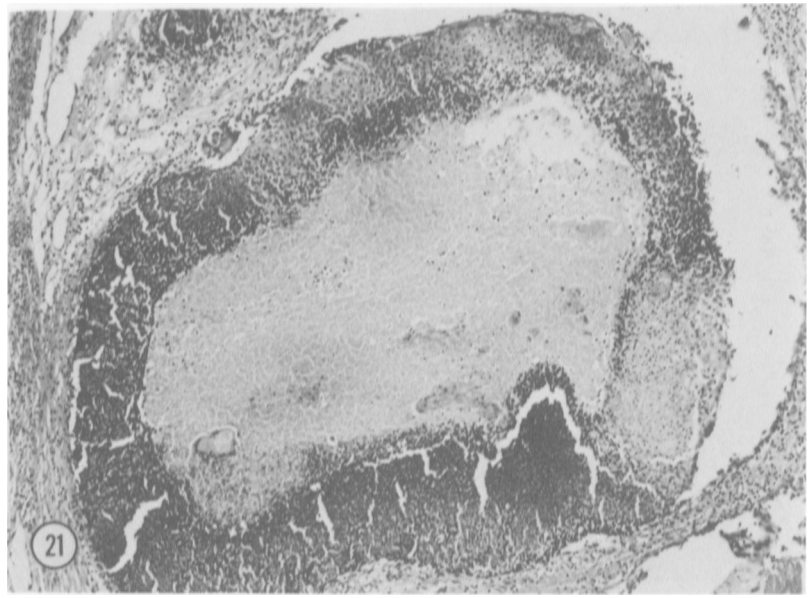
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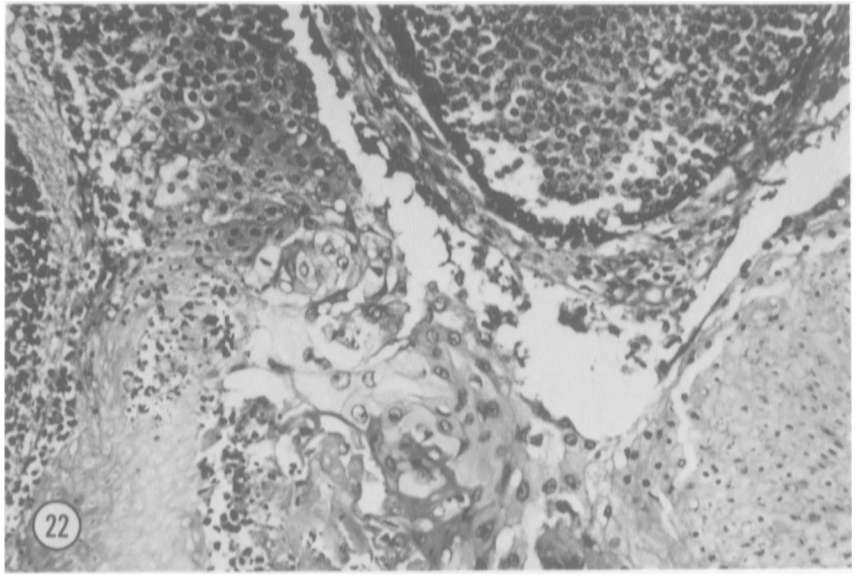
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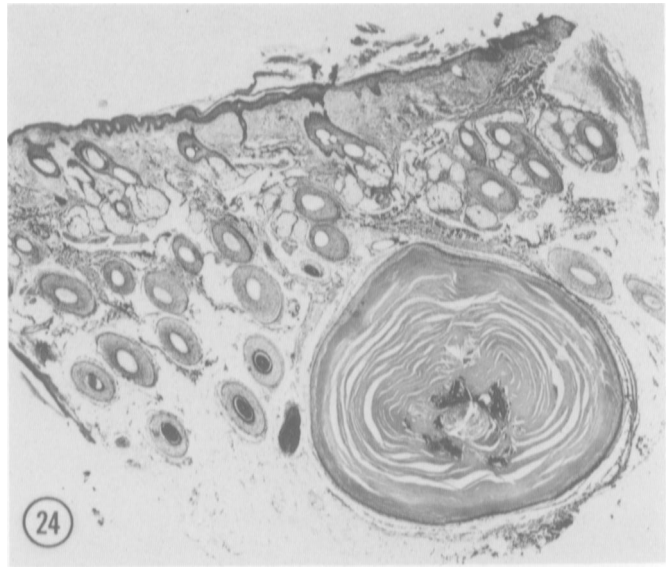
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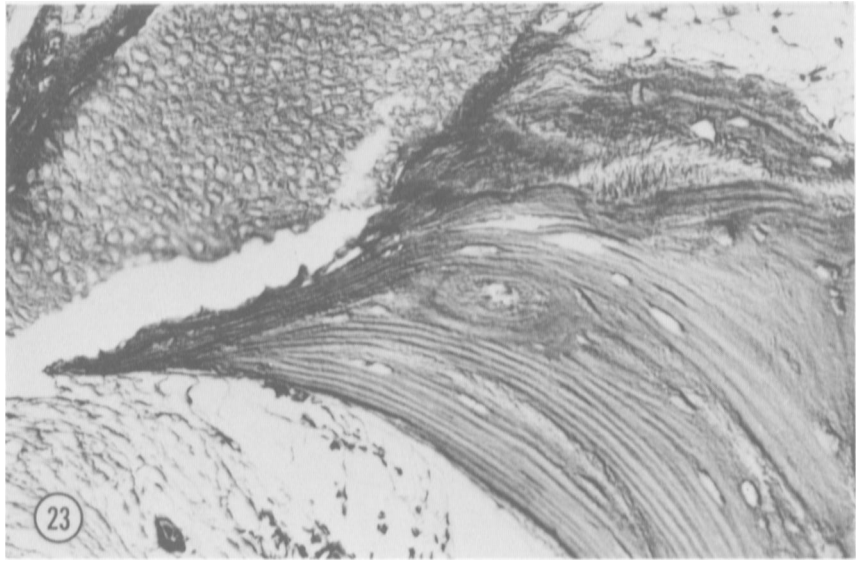
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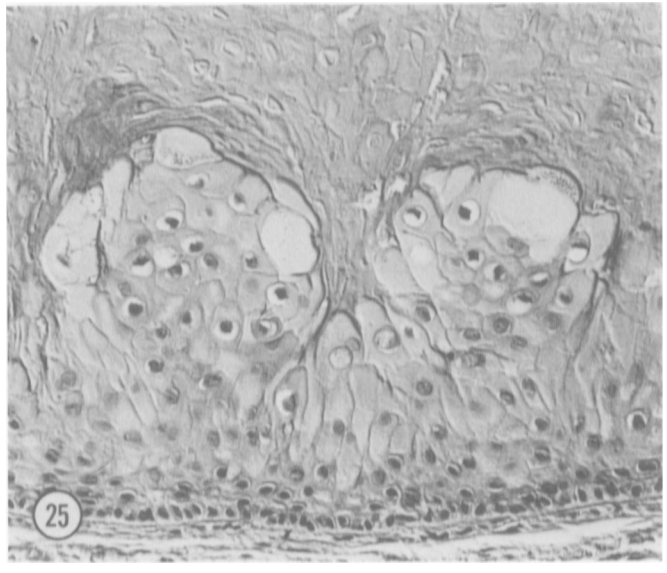
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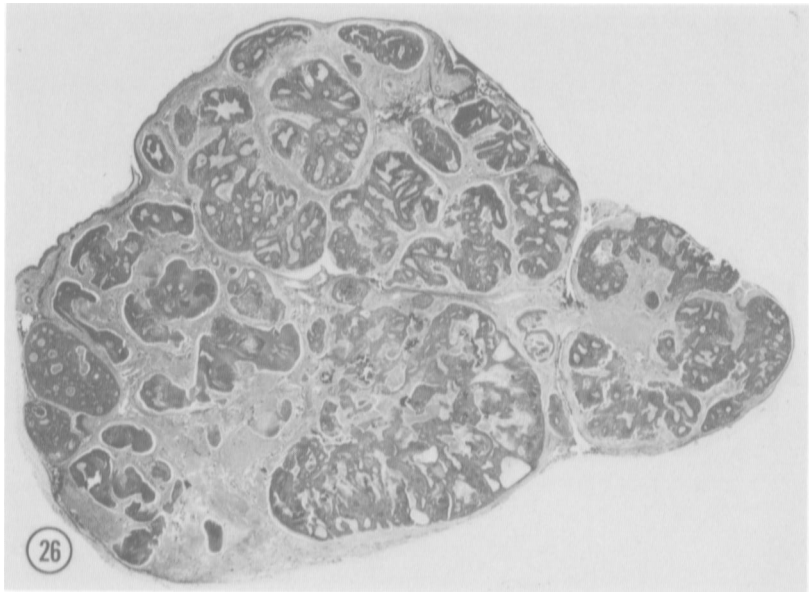
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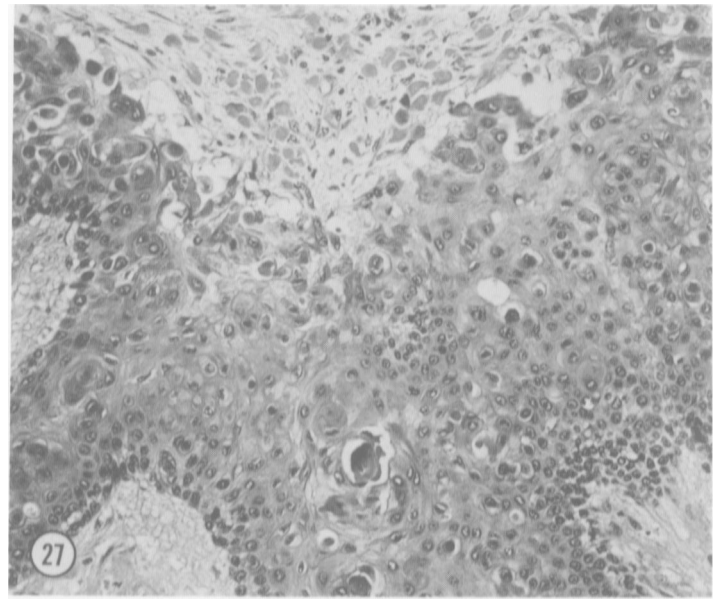
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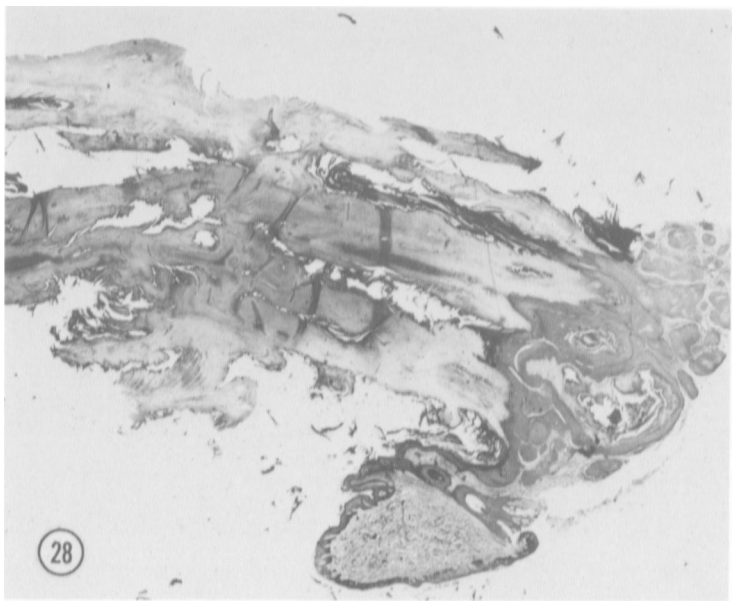
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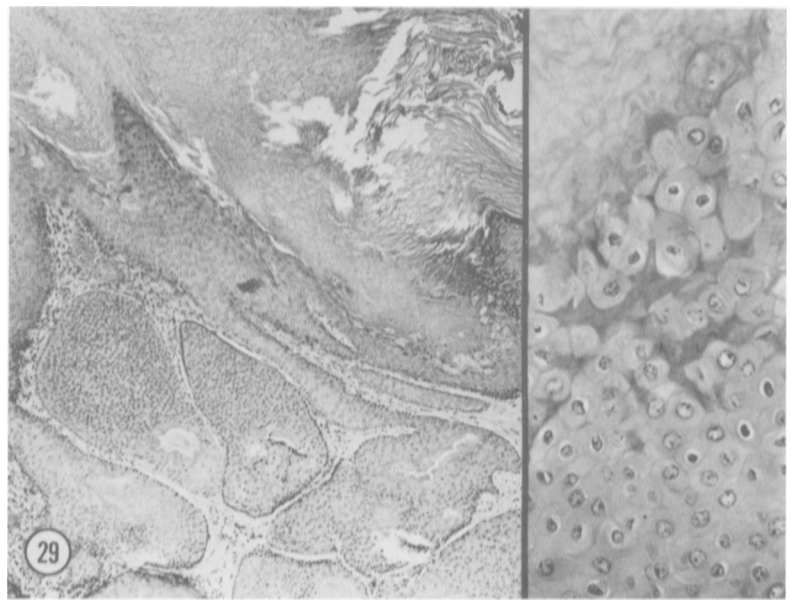
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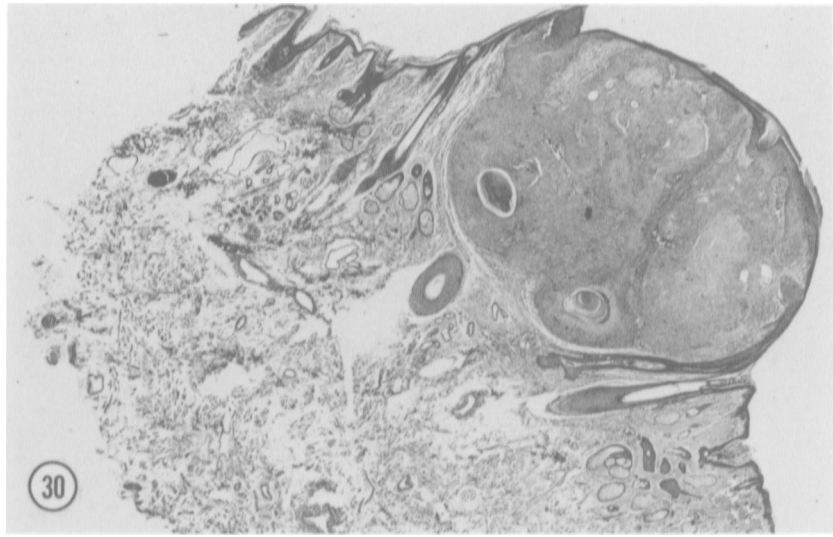
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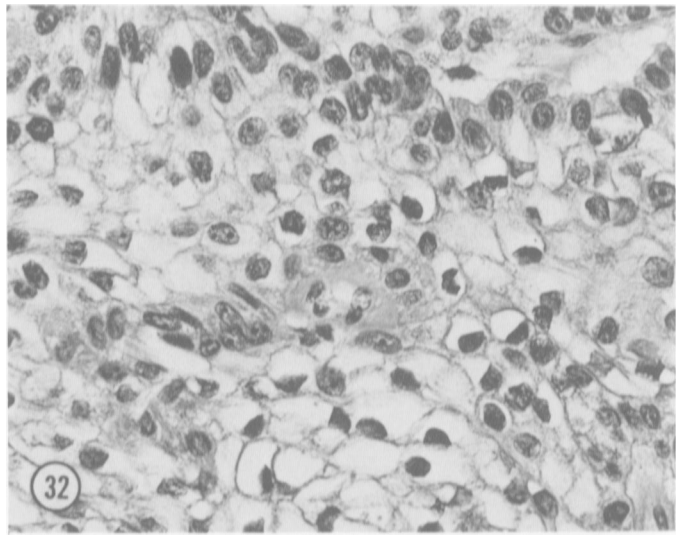
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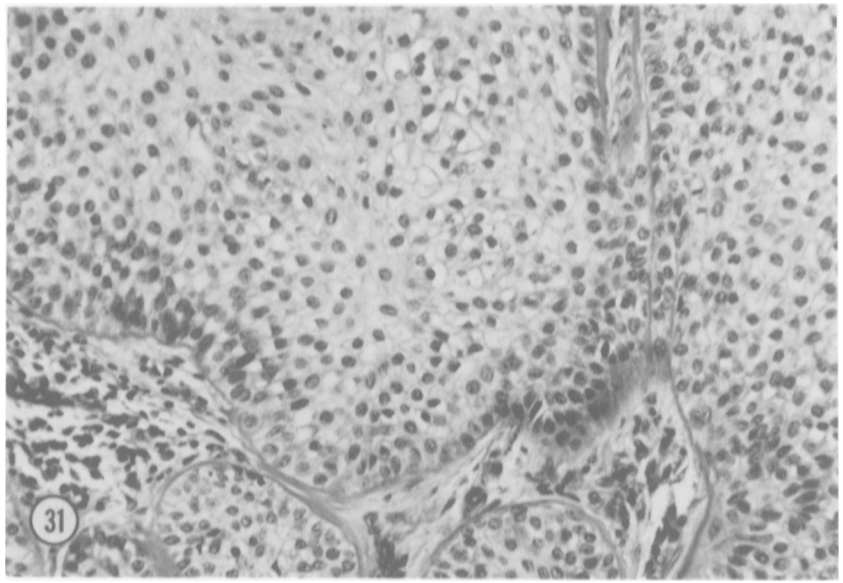
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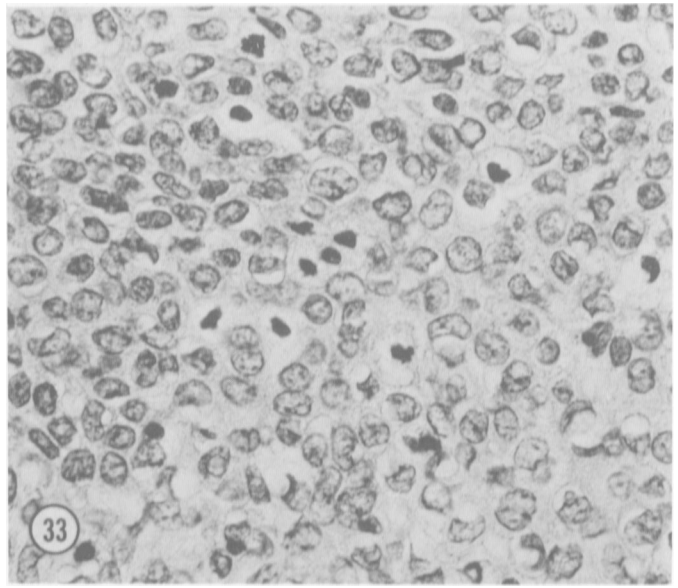
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